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EXAMINER	
RAMIREZ, DELIA M	

ART UNIT	PAPER NUMBER
1652	13

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/856,050	UEMURA ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *19,21-24,26,28 and 29* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18,20,25 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Application

Claims 1-29 are pending.

It is noted that the examination of the instant application has been assigned to a different Examiner in Group Art Unit 1652.

Applicant's election without traverse of Group I, claims 1-18, 20, 25 and 27, drawn to a protein expression vector and a host cell comprising said expression vector as well as the first claimed method of use, i.e. a process for producing a target protein using said expression vector and host cell, in Paper No. 12, filed on 8/20/2003 is acknowledged.

Claims 19, 21-24, 26, 28-29 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Specification

1. The abstract of the disclosure is objected to because of the recitation of "Tag", "cleavable nucleotide sequence", "in this order", for the reasons indicated below in Claim Rejections under 35 USC 112, second paragraph. Correction is required. See MPEP § 608.01(b).

2. The specification is objected to due to the presence of blank spaces. See page 12, line 17. Correction is required.

Priority

3. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. 119(a)-(d) to JAPAN 10/331515 filed on 11/20/1998.

4. This application is the national stage of PCT/JP99/06474 filed on 11/19/1999.

Information Disclosure Statement

5. The information disclosure statement (IDS) submitted on 5/17/2001 is acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Drawings

6. The drawings have been reviewed and are approved by a draftsperson under 37 CFR 1.84 or 1.152.

Claim Objections

7. Claims 5 and 8 are objected to due to the recitation of "nucleotide sequence encoding at least the amino acid sequence of Xaa-Xaa-Xaa…(amino acid X-Y of SEQ ID NO: X)". For clarity, it is suggested that the term be replaced with "nucleotide sequence encoding at least amino acids X-Y of SEQ ID NO: X (Xaa-Xaa-Xaa…)". Appropriate correction is required.

8. Claim 14 is objected to due to the recitation of "Host cells transformed..". For clarity and consistency, it is suggested that the term be replaced with "A host cell transformed …..". Appropriate correction is required.

9. Claims 15-17 are objected to due to the recitation of "host cells according to claim X….which are …..cells" or "host cells according to claim X wherein the ….cells are …cells". For clarity and consistency, it is suggested that the terms be replaced with "The host cell according to claim X wherein said cell is a(n) …..cell". Appropriate correction is required

Claim Rejections - 35 USC § 112, Second Paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 1-18, 20, 25 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claims 1 and 11 (claims 2-10, 12-18, 20, 25 and 27 dependent thereof) are indefinite in the recitation of "Tag sequence" for the following reasons. The term "Tag" is capitalized, therefore it is unclear if the term refers to a label/detachable fragment or if it is an acronym/special name for a type of sequence. For examination purposes, it will be assumed that it is equivalent to a "tag" or "label". Correction is required.

13. Claims 1, 3, and 6-8 (claims 2, 4-5, 9-18, 20, 25 and 27 dependent thereon) are indefinite in the recitation of "cleavable nucleotide sequence" as it is unclear if the term "cleavable" refers to the nucleotide sequence or the polypeptide encoded by it. For examination purposes, it will be assumed that the term refers to a polynucleotide which encodes a polypeptide/peptide which can be cleaved. Correction is required.

14. Claim 1 (claims 2-18, 20, 25 and 27 dependent thereon) is indefinite in the recitation of "a protein expression vector comprising a secretory nucleotide signal, ...and a cloning site into which .., in this order" as it is unclear if the term "in this order" is defining how the different parts of the vector should be assembled or if it refers to how the polynucleotide encoding the target protein is placed within the cloning site. For examination purposes, it will be assumed that the claim recites "a ...expression vector comprising (a) a secretory...(b) a polynucleotide encoding a protein tag...(c) a polynucleotide encoding a cleavable protein, and (d) a cloning site..., wherein (a), (b), (c) and (d) are assembled within the vector in the order recited". Correction is required.

15. Claim 4 (claims 5-6 dependent thereon) is indefinite in the recitation of "wherein a nucleotide sequence encoding at least one amino acid is contained as a spacer nucleotide in the 3' downstream side

of the secretory signal nucleotide sequence but in the 5' upstream side of the cleavable..." for the following reasons. First, there is no antecedent basis for a secretory signal nucleotide sequence. In addition, the language "nucleotide sequence encoding at least one amino acid is contained as a spacer nucleotide sequence in the 3' downstream side of the ...but in the 5' upstream side of .." is confusing. It is unclear as to how a sequence can be "contained as" another sequence. Also, it is unclear as to what the meaning of the term "in the 3' downstream side of ....but in the 5' upstream side of ..." within the context of the claim. For examination purposes, it will be assumed that the term recites "wherein the expression vector further comprises a polynucleotide encoding at least one amino acid wherein said polynucleotide is located between the 3' end (or downstream side) of the secretory signal and the 5' end (or upstream side) of the polynucleotide encoding a cleavable protein". Correction is required.

16. Claim 7 (claims 8-9 dependent thereon) is indefinite in the recitation of "wherein the cleavable nucleotide sequence when translated into an amino acid sequence is cleaved by an enzyme at immediate upstream and/or immediate downstream and/or in the middle of said amino acid sequence" for the following reasons. First, it is noted that it is proteins (polypeptides) and not sequences, what is cleaved by enzymes. As known in the art, a sequence is just a graphical representation of the order in which amino acids are arranged in a molecule. Second, the term "at immediate upstream and/or immediate downstream and/or in the middle of said amino acid sequence" is confusing since it is unclear as to where is the polypeptide cleaved. For examination purposes, it will be assumed that the term's meaning is "wherein the cleavable protein is cleaved by an enzyme at any location within said protein". Correction is required.

17. Claim 10 is indefinite in the recitation of "wherein the secretory signal nucleotide sequence is an IgG(k) signal or a trypsin signal" for the following reasons. First, there is no antecedent basis for the term "secretory signal nucleotide sequence". Second, it is unclear as to how a sequence can be a signal. For

examination purposes, it will be assumed that the term's intended meaning is "wherein the secretory signal is an IgG(k) or a trypsin signal". Correction is required.

18. Claim 18 is indefinite since it omits essential steps. See MPEP § 2172.01. While the claim is drawn to a method of producing a target protein, there is no indication as to how this protein is produced other than the recitation of what is used in the method, i.e. the expression vector of claim 1. No recitation of how one can use the vector to produce the protein is recited. As known in the art, vectors alone are not sufficient to produce a recombinant protein. For examination purposes, it will be assumed that the claim is directed to a method for producing a target protein wherein said method comprises cultivating host cells transformed with the vector of claim 1. Correction is required.

19. Claim 20 is indefinite since it omits essential steps and due to the recitation of "host cells according to claim 1". While the claim is drawn to a method of producing a target protein, there is no indication as to how this protein is produced other than the recitation of what is used in the method, i.e. an expression vector or host cells. It is noted that as known in the art, vectors alone can not be used to produce recombinant proteins. Furthermore, it is noted that the term "cells according to claim 1" is indefinite since claim 1 is directed to an expression vector and not to host cells. For examination purposes, it will be assumed that claim 20 is also directed to a method for producing a target protein wherein said method comprises cultivating host cells transformed with the vector of claim 1. Correction is required.

20. Claim 27 is indefinite due to the recitation of "host cells of claim 1" since claim 1 is directed to an expression vector. For examination purposes, it will be assumed that claim 27 is directed to a method for producing a recombinant fusion protein comprising cultivating the host cells of claim 14. Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

21. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

22. Claims 1-18, 20, 25 and 27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-4, 6-7, 9, 12-13 are directed to a genus of protein expression vectors wherein said vectors comprise (1) a genus of polynucleotides encoding secretion signals, (2) a genus of polynucleotides encoding protein tags, and (3) a genus of polynucleotides encoding cleavable proteins. Claims 5 and 8 are directed to the an expression vector which comprises a genus of polynucleotides encoding secretion signals, a genus of polynucleotides encoding protein tags, and polynucleotides encoding specific peptides. Claim 10 is directed to the expression vector of claim 1 further comprising specific secretion signals. Claim 11 is directed to the expression vector of claim 1 further comprising a polynucleotide encoding a polyhistidine tag. Claims 14-17 are drawn to host cells comprising the expression vector of claim 1, whereas claims 18, 20, 25 and 27 are drawn to a method of producing any recombinant protein with host cells transformed with the expression vector of claim 1.

The specification discloses (1) the mouse Ig kappa chain secretion signal of pSecTag2A (Invitrogen) as set forth in amino acids 1-21 of SEQ ID NO: 17, (2) the trypsin signal set forth in amino acids 1-23 of SEQ ID NO: 19, (3) the histidine tags set forth in amino acids 35-40 of SEQ ID NO: 17 and 30-35 of SEQ ID NO: 19, (4) the cleavable peptides set forth in amino acids 24-29 of SEQ ID NO: 19, 36-40 of SEQ ID NO: 19 and 41-45 of SEQ ID NO: 17, and (5) the neurosin of SEQ ID NO: 15. However, the specification fails to disclose other secretion signals, protein tags, cleavable peptides and

cleaving agents specific for such cleavable peptides which can be used to recombinantly produce any protein. While many secretion signals, protein tags, and cleavable peptides and their corresponding cleaving agents are known in the art, one cannot reasonably conclude that the claimed invention is adequately described since not all secretion signals are functional for the recombinant production of any protein in any host cell. Furthermore, the specification does not disclose the critical structural elements required in any secretion signal to be functional in any host cell, the structural elements of all cleavable peptides along with the corresponding cleavable agent, or the structural elements of any protein tag. The specification only discloses a few species of the genera of polynucleotides encoding secretion signals, protein tags, and cleavable proteins required to construct the genus of vectors claimed which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of the claimed invention. Thus, one skilled in the art cannot reasonably conclude that Applicant had possession of the claimed invention at the time the instant application was filed.

23. Claims 1-18, 20, 25 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for (a) an expression vector comprising (1) the polynucleotide of SEQ ID NO: 16, which encodes the mouse Ig kappa chain secretion signal, a histidine tag, a cleavable peptide, and a spacer, as well as the polynucleotide of SEQ ID NO: 14 encoding neurosin, or (2) the polynucleotide of SEQ ID NO: 18, which encodes a trypsin secretion signal, a histidine tag, a cleavable peptide and a spacer, as well as the polynucleotide of SEQ ID NO: 14 encoding neurosin, (b) host cells transformed with the vectors of (1) or (2), and (c) a method to produce the neurosin of SEQ ID NO: 18 said method comprising cultivating the host cells of (b), does not reasonably provide enablement for an expression vector comprising sequences encoding any secretory signal, any protein tag, any cleavable peptide, and any protein. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims as described above, is not commensurate with the enablement provided in regard to the large number of unknown secretion signals, protein tags, cleavable peptides, cleaving agents specific for such cleavable peptides, and proteins encompassed by the claims. While the specification discloses (1) the mouse Ig kappa chain secretion signal of pSecTag2A (Invitrogen) as set forth in amino acids 1-21 of SEQ ID NO: 17, (2) the trypsin signal set forth in amino acids 1-23 of SEQ ID NO: 19, (3) the histidine tags set forth in amino acids 35-40 of SEQ ID NO: 17 and 30-35 of SEQ ID NO: 19, (4) the cleavable peptides set forth in amino acids 24-29 of SEQ ID NO: 19, 36-40 of SEQ ID NO: 19 and 41-45 of SEQ ID NO: 17, and (5) the neurosin of SEQ ID NO: 15, the specification fails to disclose other secretion signals, protein tags, cleavable peptides and cleaving agents specific for such cleavable peptides which can be used to recombinantly produce any protein. While many secretion signals, protein tags, and cleavable peptides and their corresponding cleaving agents are known in the art, not all secretion signals are adequate for the recombinant production of any protein in any host cell. Furthermore, the specification does not disclose the critical structural elements required in any secretion signal to be functional in any host cell or the structural elements of all cleavable peptides along with the corresponding cleavable agent. Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge the structure of other secretions signals, cleavable peptides/cleaving agents, and protein tags required to recombinantly produce any protein, one of ordinary

skill in the art would have to go through the burden of undue experimentation in order to isolate/make all the secretion signals, cleavable peptides/cleaving agents, and protein tags, as encompassed by the claim, and further determine which ones can be used in a particular host cell to recombinantly produce the desired protein. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

24. Claims 1-4, 6, 7, 14, 18, 20, 25, 27 are rejected under 35 U.S.C. 102(b) as being anticipated by the New England Biolabs 1995 catalog. As indicated in Paper No. 11, mailed on 8/12/2003, the New England Biolabs 1995 catalog teaches a protein expression vector (pMAL-p2) comprising a nucleotide sequence encoding a secretion signal (that of malE), a nucleotide sequence encoding a protein tag (maltose binding protein; MBP) used for purification, a nucleotide sequence encoding a spacer of 10 asparagine residues, a nucleotide sequence encoding a cleavable peptide (Factor Xa cleavage site, Ile-Glu-Gly-Arg), and a multiple cloning site (page 140, column 1; top figure on page 141). In addition, the New England Biolabs 1995 catalog teaches an E. coli host cell transformed with the expression vector (top figure, page 140) and the production of a fusion protein containing MBP and paramyosin, as shown in the SDS-PAGE diagram of page 140 and its corresponding legend.

Claim 1 is directed to a protein expression vector comprising a nucleotide sequence encoding any secretion signal, any protein tag, any cleavable polypeptide, and a cloning site to insert a polynucleotide

encoding any protein. pMAL-p2 comprises a nucleotide sequence encoding the malE secretion signal, the nucleotide sequence encoding MBP (purification tag), a nucleotide sequence encoding the Factor Xa cleavage site, and a multiple cloning site, therefore anticipating claim 1 as written. Claim 2 is directed to the expression vector of claim 1 with the added limitation that the vector also comprises a polynucleotide encoding a target protein within the cloning site. Therefore, the pMAL-p2 vector used to transform E. coli cells to produce the MBP-paramyosin fusion protein anticipates this claim as written. Claim 3 is directed to the expression vector of claim 1 wherein either the cloning site or the polynucleotide encoding the protein is present successively at the 3' end of the polynucleotide encoding the cleavable polypeptide. Since the cloning site in pMAL-p2 is located after the polynucleotide encoding the Factor Xa cleavage site, this claim is also anticipated. Claim 4 is directed to the expression vector of claim 1 with the added limitation that a polynucleotide encoding a spacer is located between the secretion signal's polynucleotide and the cleavable protein's polynucleotide. Therefore, the 10 asparagine-residue spacer in pMAL-p2 anticipates the claim as written. Claim 6 is directed to the expression vector of claim 4 with the added limitation that the spacer contains a cleavable polypeptide, therefore it is anticipated by pMAL-p2 as described above. Claim 7 is directed to the expression vector of claim 1 wherein the cleavable polypeptide can be cleaved at any location, therefore the Factor Xa cleaving site in pMAL-p2 anticipates this claim as written. Claim 12 is directed to the expression vector of claim 1 further comprising a nucleotide sequence encoding an antibody recognition epitope. Since the New England Biolabs 1995 catalog also teaches a rabbit antiserum against MBP in page 141, the polynucleotide encoding MBP would also be a polynucleotide encoding an antibody recognition epitope, therefore the teachings of the New England Biolabs 1995 catalog would anticipate the claim as written. Claim 14 is directed to host cells transformed with the expression vector of claim 1, therefore the E. coli host cells described in page 140 as discussed above, anticipate the claim as written. Claims 18, 20, 25 and 27 are directed to a method to produce any protein by cultivating a host cell transformed with the expression vector of claim 1.

Therefore, the production of a MBP-paramyosin fusion protein by cultivation of E. coli host cells transformed with pMAL-p2 anticipate the claims as written.

Claim Rejections - 35 USC § 103

25. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

26. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

27. Claims 8, 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the New England Biolabs 1995 catalog in view of the Invitrogen 1997 product catalog. The teachings of the New England Biolabs 1995 catalog have been described above. The pMAL-p2 vector of New England Biolabs does not comprise a nucleotide sequence encoding a polyhistidine tag, the peptide set forth in amino acids 36-40 of SEQ ID NO: 19 (DDDK), or a cleavable peptide wherein the peptide is cleaved by enterokinase. The Invitrogen 1997 catalog teaches the pRSET A, B, C vectors for expression in prokaryotic host cells (page 37). These vectors all comprise the nucleotide sequence encoding the enterokinase cleavage site (page 37) which contains the peptide DDDK (page 12, second column, first paragraph). pRSET A, B, C

also contain the nucleotide sequence encoding a polyhistidine tag (His6). The Invitrogen 1997 catalog does not teach the pMAL-p2 vector.

Claims 8, 9 and 11 are drawn to the expression vector of claim 7 or 1 wherein (1) the cleavable peptide comprises amino acids 36-40 of SEQ ID NO: 19, (2) the enzyme used to cleave the cleavable polypeptide is enterokinase, and (3) the protein tag is a polyhistidine tag, respectively.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make an expression vector, as taught by the New England Biolabs 1995 catalog, wherein the cleavable peptide is the enterokinase cleavage site (DDDK) and wherein the expression vector further comprises a nucleotide sequence encoding a polyhistidine tag. A person of ordinary skill in the art is motivated to construct such a vector because the target protein may contain the Factor Xa cleavage site. As such, another cleavable peptide would be required to obtain a full length protein. In addition, one is motivated to add a polyhistidine tag for the benefit of having an additional purification tag which would enhance the purity of the desired protein. An amylose column can be used to purify the fusion protein (MBP-desired protein) and metal affinity chromatography can be used to further purify either the fusion protein or the desired protein once is cleaved from MBP. One of ordinary skill in the art has a reasonable expectation of success at making the vector since the New England Biolabs 1995 catalog teaches the pMAL-p2 vector and the Invitrogen 1997 catalog teaches prokaryotic expression vectors comprising nucleotides sequences encoding polyhistidine tags and the enterokinase cleavage site DDDK. Furthermore, the use of a histidine tag and the enterokinase cleavage site for recombinant protein production is well known and widely used in the art. Therefore, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Conclusion

28. No claim is in condition for allowance.

29. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
October 30, 2003

REBECCA E. PRUTY
PRIMARY EXAMINER
1600